

October 17, 2003

Preliminary Amendment

This listing of claims will replace all prior versions, and listings, of claims in the application:  
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LISTING OF CLAIMS:

1. – 15. (Cancelled)

16. (New) A method for identification of underperfused regions in a human or animal patient which comprises administering an effective amount of a nitrogen-containing cascade polymer having complexing ligands which complex at least 16 ions of an element of atomic numbers 20-29, 39, 42, 44 or 57-83, and performing NMR diagnosis on the patient to identify the underperfused regions, wherein the nitrogen-containing cascade polymer having complexing ligands is of the following formula (I):

$$A - \{X - [Y - (Z - (W - K_w)_z)_y]_x\}^a \quad (I),$$

in which

A stands for a nitrogen-containing cascade nucleus of base multiplicity a;  
 X and Y, independently of one another, stand for a direct bond or a cascade reproduction unit

of reproduction multiplicity x or y;

Z and W, independently of one another, stand for a cascade reproduction unit of reproduction

multiplicity z or w;

a stands for numbers 2 to 12;

x, y, z, and w, independently of one another, stand for numbers 1 to 4,

provided that the product of the multiplicities,

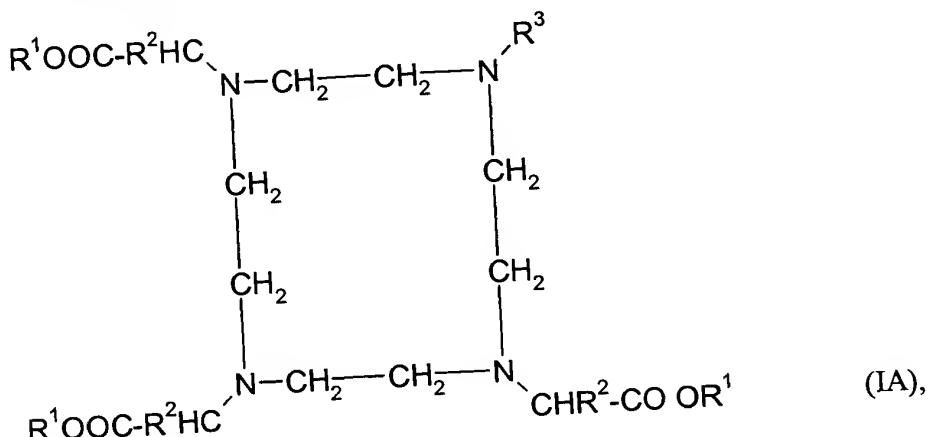
$$16 \leq a \cdot x \cdot y \cdot z \cdot w \leq 64$$

holds true;

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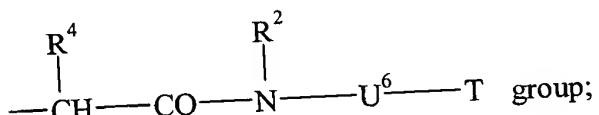
**K** stands for the radical of a complexing agent of the formula (IA):



in which  $\text{R}^1$ , independently of one another, stand for a hydrogen atom or a metal ion equivalent of atomic numbers 20-29, 39, 42-44 or 57-83, provided that at least 16 of the total  $\text{R}^1$  groups are ions of an element of atomic numbers 20-29, 39, 42, 44 or 57-83;

**R**<sup>2</sup> stands for a hydrogen atom, or a methyl or an ethyl radical, which optionally is substituted with 1-2 hydroxy or 1 carboxy group(s);

**R**<sup>3</sup> stands for a



**R**<sup>4</sup> stands for a straight-chain, branched, saturated or unsaturated C<sub>1</sub>-C<sub>30</sub> alkyl chain, which optionally is interrupted by 1-10 oxygen atoms, 1 phenylene group, 1 phenylenoxy group and/or optionally substituted by 1-5 hydroxy, 1-3 carboxy, 1-phenyl group(s);

**R**<sup>5</sup> stands for a hydrogen atom or for R<sup>4</sup>;

U<sup>6</sup>

stands for a straight-chain, branched, saturated or unsaturated C<sub>1</sub>-C<sub>20</sub> alkylene group optionally containing 1-5 imino, 1-3 phenylene, 1-3 phenylenoxy, 1-3 phenylenimino, 1-5 amide, 1-2 hydrazide, 1-5 carbonyl, 1-5 ethylenoxy, 1 urea, 1 thiourea, 1-2 carboxyalkylimino, 1-2 ester groups; 1-10 oxygen, 1-5 sulfur and/or 1-5 nitrogen atom(s) and/or optionally substituted by 1-5 hydroxy, 1-2 mercapto, 1-5 oxo, 1-5 thioxo, 1-3 carboxy, 1-5 carboxyalkyl, 1-5 ester and/or 1-3 amino group(s), whereby the phenylene groups that are optionally contained can be substituted by 1-2 carboxy, 1-2 sulfo or 1-2 hydroxy groups;

T

stands for a -CO- $\alpha$ , -NHCO- $\alpha$  or -NHCS- $\alpha$  group; and

$\alpha$

stands for the bonding site to the terminal nitrogen atoms of the last generation, of reproduction unit W; and

wherein, optionally, non-complexed acid hydrogen atoms are replaced by one or more cations of inorganic and/or organic bases, amino acids or amino acid amides, and optionally, any terminal amino groups are acylated.

17. (New)

The method of claim 16, wherein the nitrogen-containing cascade polymer with complexed complexing ligands has a molecular weight of 10,000 to 80,000 daltons.

18. (New)

The method of claim 16, wherein the method is for identification of underperfused regions in the myocardium of the patient.

19. (New) The method of claim 16, wherein the at least 16 ions of an element of atomic numbers 20-29, 39, 42, 44 or 57-83 are Gd ions.

20. (New) The method of claim 16, wherein the K radicals of formula (IA) are 1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane radicals wherein at least 16 are complexed with ions of an element of atomic numbers 20-29, 39, 42, 44 or 57-83.

21. (New) The method of claim 20, wherein the at least 16 ions of an element of atomic numbers 20-29, 39, 42, 44 or 57-83 are Gd ions.

22. (New) The method of claim 16, wherein, in formula (I), A is trimesic acid triamide.

23. (New) The method of claim 20, wherein, in formula (I), A is trimesic acid triamide.

24. (New) The method of claim 16, wherein the nitrogen-containing cascade polymer has 2-(trilysylamino)-ethyl repeating units.

25. (New) The method of claim 20, wherein the nitrogen-containing cascade polymer has 2-(trilysylamino)-ethyl repeating units.

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## 26. (New)

The method of claim 20, wherein the nitrogen-containing cascade polymer having complexing ligands which complex at least 16 ions of an element of atomic numbers 20-29, 39, 42, 44 or 57-83 is a 24-mer-Gd-complex of N-(5-(1,4,7-tris(carboxymethyl)-1,4,7,10-tetraazacyclododecane)-yl-4-oxo-3-azahexanoyl)-cascade polyamide based on N,N,N',N', N'', N''-hexakis[2-(tritylsylamino)-ethyl]-trimesic acid triamide.

## 27. (New)

An angiography method for diagnosis of vascular disease in a human or animal patient which comprises administering an effective amount of a nitrogen-containing cascade polymer having complexing ligands which complex at least 16 ions of an element of atomic numbers 20-29, 39, 42, 44 or 57-83, and performing an angiography diagnosis on the patient, wherein the nitrogen-containing cascade polymer having complexing ligands is of the following formula:

$$A-\{X-[Y-(Z-(W-K_w)_z)_y]_x\}^a \quad (I),$$

in which

A stands for a nitrogen-containing cascade nucleus of base multiplicity a; X and Y, independently of one another, stand for a direct bond or a cascade reproduction unit of reproduction multiplicity x or y;

Z and W, independently of one another, stand for a cascade reproduction unit of reproduction multiplicity z or w;

a stands for numbers 2 to 12;

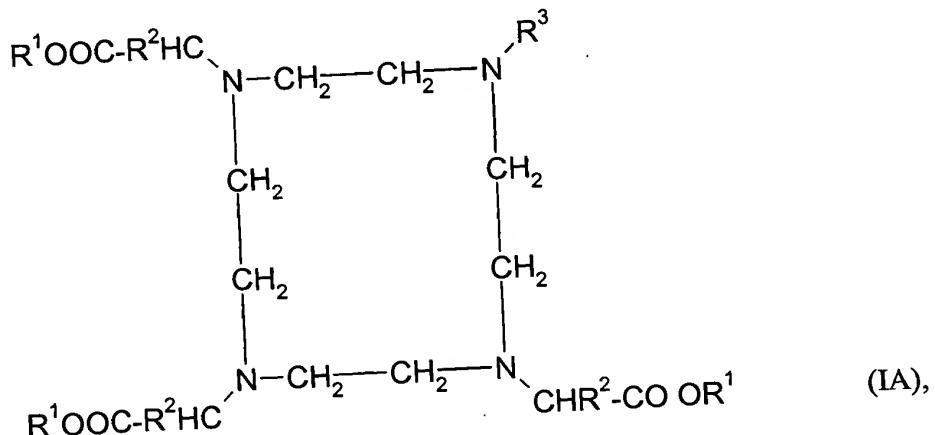
x, y, z, and w, independently of one another, stand for numbers 1 to 4,

provided that the product of the multiplicities,

$$16 \leq a \cdot x \cdot y \cdot z \cdot w \leq 64$$

holds true;

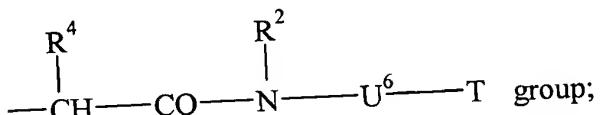
K stands for the radical of a complexing agent of the formula (IA):



in which R<sup>1</sup>, independently of one another, stand for a hydrogen atom or a metal ion equivalent of atomic numbers 20-29, 39, 42, 44 or 57-83, provided that at least 16 of the total R<sup>1</sup> groups are ions of an element of atomic numbers 20-29, 39, 42, 44 or 57-83;

R<sup>2</sup> stands for a hydrogen atom, or a methyl or an ethyl radical, which optionally is substituted with 1-2 hydroxy or 1 carboxy group(s);

R<sup>3</sup> stands for a



R<sup>4</sup> stands for a straight-chain, branched, saturated or unsaturated C<sub>1</sub>-C<sub>30</sub> alkyl chain, which optionally is interrupted by 1-10 oxygen atoms, 1 phenylene group, 1 phenoxy group and/or optionally substituted by 1-5 hydroxy, 1-3 carboxy, 1-phenyl group(s);

R<sup>5</sup> stands for a hydrogen atom or for R<sup>4</sup>;

U<sup>6</sup> stands for a straight-chain, branched, saturated or unsaturated C<sub>1</sub>-C<sub>20</sub> alkylene group optionally containing 1-5 imino, 1-3 phenylene, 1-3 phenoxy, 1-3 phenylenimino, 1-5 amide, 1-2 hydrazide, 1-5 carbonyl, 1-5 ethylenoxy, 1-5 urea, 1 thiourea, 1-2 carboxyalkylimino, 1-2 ester groups; 1-10 oxygen, 1-5 sulfur and/or 1-5 nitrogen atom(s) and/or optionally substituted by 1-5 hydroxy, 1-2 mercapto, 1-5 oxo, 1-5 thioxo, 1-3 carboxy, 1-5 carboxyalkyl, 1-5 ester and/or 1-3 amino group(s), whereby the phenylene groups that are optionally contained can be substituted by 1-2 carboxy, 1-2 sulfo or 1-2 hydroxy groups;

T stands for a -CO- $\alpha$ , -NHCO- $\alpha$  or -NHCS- $\alpha$  group; and

$\alpha$  stands for the bonding site to the terminal nitrogen atoms of the last generation, of reproduction unit W; and

wherein, optionally, non-complexed acid hydrogen atoms are replaced by one or more cations of inorganic and/or organic bases, amino acids or amino acid amides, and optionally, any terminal amino groups are acylated.

28. (New) The method of claim 16, wherein the nitrogen-containing cascade polymer with complexed complexing ligands has a molecular weight of 10,000 to 80,000 daltons.